

### **REMARKS/ARGUMENTS**

By this Amendment, claim 39 is added. Claims 1 and 39 are pending.

Citations to the Specification are directed to U.S. Patent Application Publication No. 2006/0128703 (Dodda Mohan Rao). Support for claim 39 can be found throughout the Specification as filed, and specifically: Example 2 ([0049]) discloses the conversion of linezolid form II into linezolid form III, with an enantiomeric excess of 99.8%. In addition, Example 3 ([0050]) discloses the conversion of linezolid to linezolid form III, with 97% enantiomeric excess, and Example 4 ([0051]) discloses linezolid form III with an enantiomeric excess of 96%. Additionally, Example 5 ([0052]) discloses linezolid form III with an enantiomeric excess of 95%. Thus the Specification supports the limitation "at least a 99.8% enantiomeric excess of linezolid form III". No new matter is added by this amendment.

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

### **Art Rejections**

Claim 1 stands rejected as anticipated or obvious over Barbachyn et al., U.S. Patent No. 5,688,792. Claim 1 stands rejected as anticipated or obvious over Meng. Claim 1 stands rejected as anticipated or obvious over Pearlman et al. Applicant respectfully traverses these rejections. Since the Examiner has previously considered these rejections together, they will be addressed together, herein.

The Examiner argues that for the reasons provided in the office action dated May 22, 2008, it is maintained that IR data is insufficient to unambiguously distinguish different polymorphic forms. In the May 22, 2008 Office Action, the Examiner argues that IR data is not sufficient to unambiguously show that the cited prior art solid form are indeed different from the

instantly claimed invention.

With regard to the anticipation rejection, in Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987) (MPEP 2131), the CAFC set forth that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference". In the instant case, not every element of the claims is present in the Barbachyn, Meng, or Pearlman reference.

If the claims are rejected as being obvious over any one of Barbachyn, Meng, or Pearlman, the claims are patentable over the Barbachyn, Meng, or Pearlman references for the following reasons. The framework for the objective analysis for determining obviousness under 35 U.S.C. 103 is stated in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966). Obviousness is a question of law based on underlying factual inquiries. The factual inquiries enunciated by the Court are as follows: (A) Determining the scope and content of the prior art; and (B) Ascertaining the differences between the claimed invention and the prior art; and (C) Resolving the level of ordinary skill in the pertinent art. To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. In re Royka, 490 F.2d 981 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." In re Wilson, 424 F.2d 1382, 1385 (CCPA 1970). MPEP 2143.03. It is important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. (KSR v Teleflex, 12 S.Ct. 1727, 1740 (US 2007)). Here, the Barbachyn, Meng, and/or Pearlman references do not teach or suggest all the limitations of the claims.

Claim 1 is directed to a crystalline linezolid form III, characterized by an x-ray powder diffraction spectrum having peaks expressed as 2 $\theta$  at about 7.6, 9.6, 13.6, 14.9, 18.2, 18.9, 21.2,

22.3, 25.6, 26.9, 27.9 and 29.9 degrees, and further characterized by an IR spectrum having main bands at about 3338, 1741, 1662, 1544, 1517, 1471, 1452, 1425, 1400, 1381, 1334, 1273, 1255, 1228, 1213, 1197, 1176, 1116, 1082, 1051, 937, 923, 904, 869, 825 and 756  $\text{cm}^{-1}$ , wherein there is at least a 99.8% enantiomeric excess of the linezolid form III. The Examiner argues that the prior art form is encompassed by the instant claims, and that the presence of distinct XR data may not be sufficient to establish a difference in the crystalline form, allegedly because it is well known in the art that purity affects spectral/RD data.

As shown in the Response of August 20, 2008, the art teaches that XRPD data is reliable to differentiate between different polymorphic crystalline forms, and that the art teaches that IR data is reliable to differentiate between crystalline polymorphic forms. Applicant has provided XRPD data and IR spectra for the claimed polymorphic form, and demonstrated that IR data show the polymorphic forms as taught in the Barbachyn, Meng, and Pearlman references are distinct from the claimed polymorphic form III linezolid.

In the Office Action of November 8, 2007, with regard to the rejections over Barbachyn, Meng, and Pearlman, the Examiner requested that Applicant provide a showing of how the instantly claimed crystalline form is different from the disclosures of Barbachyn, Meng, and Pearlman (see Office Action of November 8, 2008 at pages 5-6).

The Examiner's attention is directed to U.S. Patent No. 6,559,305 (Bergren), cited on the Information Disclosure Statement submitted October 17, 2005. The '305 patent discloses the relation (and identity) between the linezolid originally produced (i.e. the product obtained as per US 5,688,792) and Form II. The '305 patent discloses that several crystalline forms of linezolid are known in the art, and sets forth the IR spectra for several of the forms. According to the '305 patent (see '305, column 2, lines 43-45):

When linezolid was originally produced, the crystal form was Form I. Form II differs from Form I in its IR spectrum, X-ray powder diffraction spectrum and melting point.

The '305 patent further discloses that IR data of Form I was used to differentiate Form II from Form I, see '305, (column 1, lines 26-27 (Form I) and column 2, lines 13-15 (Form II)).

In addition, the IR spectral bands of Form I reported in U.S. Patent No. 6,559,305 are same as that reported in the Brickner et al. reference (J. Med. Chem., 39(3), 673-9 (1996)), cited in the Information Disclosure Statement submitted October 17, 2005, at page 678:

This was purified on a medium pressure silica gel column (5.5 cm x 34 cm eluted with concentration gradient of 3-10% methanol-ethyl acetate), to give upgraded material This was again submitted to chromatography and then recrystallized from ethyl acetate and hexanes to give 11.244 g (68.8% yield from 5b) of U-100766 as white crystals. mp=181.5-182.5°C... IR (mineral oil mull, cm<sup>-1</sup>): 3284, 3092, 1753, 1728, 1649, 1565, 1519, 1447, 1435.

Accordingly, the art teaches the difference between Form I and Form II linezolid. A comparison of the XRPD and IR data for the instantly claimed Form III linezolid shows that the instantly claimed form is clearly distinct from Form I or Form II linezolid as taught in the art.

In addition, Applicant submits herewith the First Declaration under 1.132 of D. Mohan Rao, Ph.D., which sets forth the DSC thermogram of linezolid Form III and as a comparison the DSC thermogram of linezolid form II. As can be seen in **Appendix 1 - C** of the Declaration, linezolid form II has peaks at 155.32 °C and 179.06°C. In contrast linezolid form III has a single peak at 178.96 °C (First Declaration under 1.132 of D. Mohan Rao, Ph.D., **Appendix 1 - B**). Accordingly, form II and form III linezolid are different polymorphic forms with different melting temperatures (see First Declaration under 1.132 of D. Mohan Rao, Ph.D., ¶19).

The art teaches that linezolid has a melting point of 181.5-182.5°C (see Merck Index,

Thirteenth Edition, 2001, page 986, No. 5526, cited on the Information Disclosure Statement, submitted herewith). In contrast linezolid form III has a melting point of 178.96 °C (see First Declaration under 1.132 of D. Mohan Rao, Ph.D., **Appendix 1 - B**, see ¶16).

Here, the claims set forth the XRPD data and IR spectra for the claimed linezolid polymorphic Form III, and the claimed Form III linezolid is clearly different from the forms as disclosed in any of the Barbachyn, Meng, or Pearlman references. Applicant has demonstrated that XRPD and IR data show the polymorphic forms as taught in the Barbachyn, Meng, and Pearlman references are distinct from the claimed polymorphic form III linezolid. In addition, Applicant has provided a comparison of the DSC thermogram for the claimed linezolid form III polymorph and linezolid form II polymorph, and shown that the melting temperature for linezolid form III is different than that reported in the art for linezolid. Therefore, the assumption that crystallization of linezolid according to the methods as disclosed in Barbachyn, Meng, and Pearlman will yield the same polymorphic form as crystallization according to the method as set forth in the instant application has no basis in fact. Thus, the claimed crystalline Form III linezolid is not disclosed or suggested in any of the Barbachyn, Meng, or Pearlman references.

Accordingly, reconsideration and withdrawal of the rejection of claim 1 under 35 USC 102(b) and/or 35 USC 103(a) is respectfully requested.

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Application No. 10/524,478  
Amendment Dated 6/4/2009  
Reply to Office Action of 03/19/2009

For at least the reasons set forth above, it is respectfully submitted that the above-identified application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are respectfully requested.

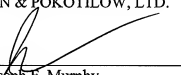
Should the Examiner believe that anything further is desirable in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,

CAESAR, RIVISE, BERNSTEIN,  
COHEN & POKOTILOW, LTD.

June 4, 2009

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